Self-Assembly of Artificial Actin Filaments

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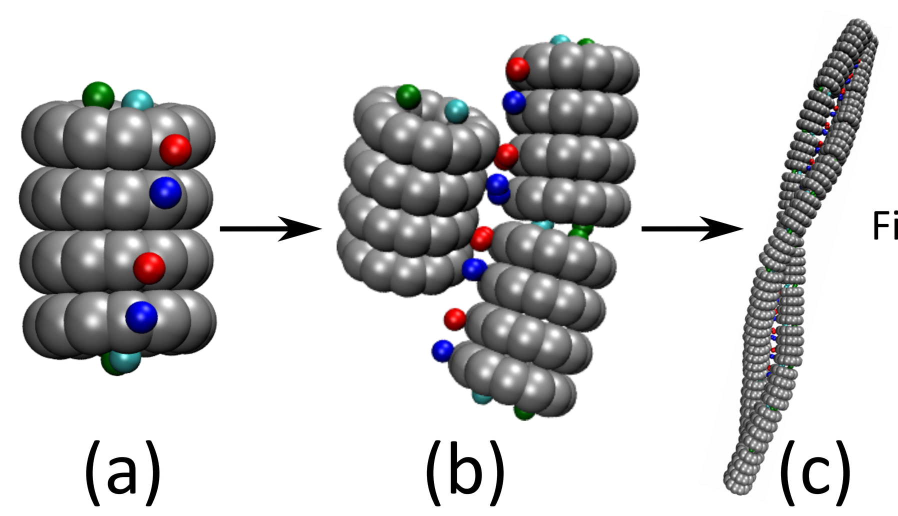
❑ Motivation

- Actin filaments, or microfilaments, are long (~ several μm), double-stranded, helical filaments that span the cytoplasm of cells.
- Typical diameter only ~6 nm across, but have a pitch length (distance for one full "twist" of double helix) of ~72 nm.[1]
- Important for cell mobility and cell division, but assembly mechanism still not well understood.
- How do we make double-stranded helical structures that mimic microfilaments such that we can study the self-assembly process?

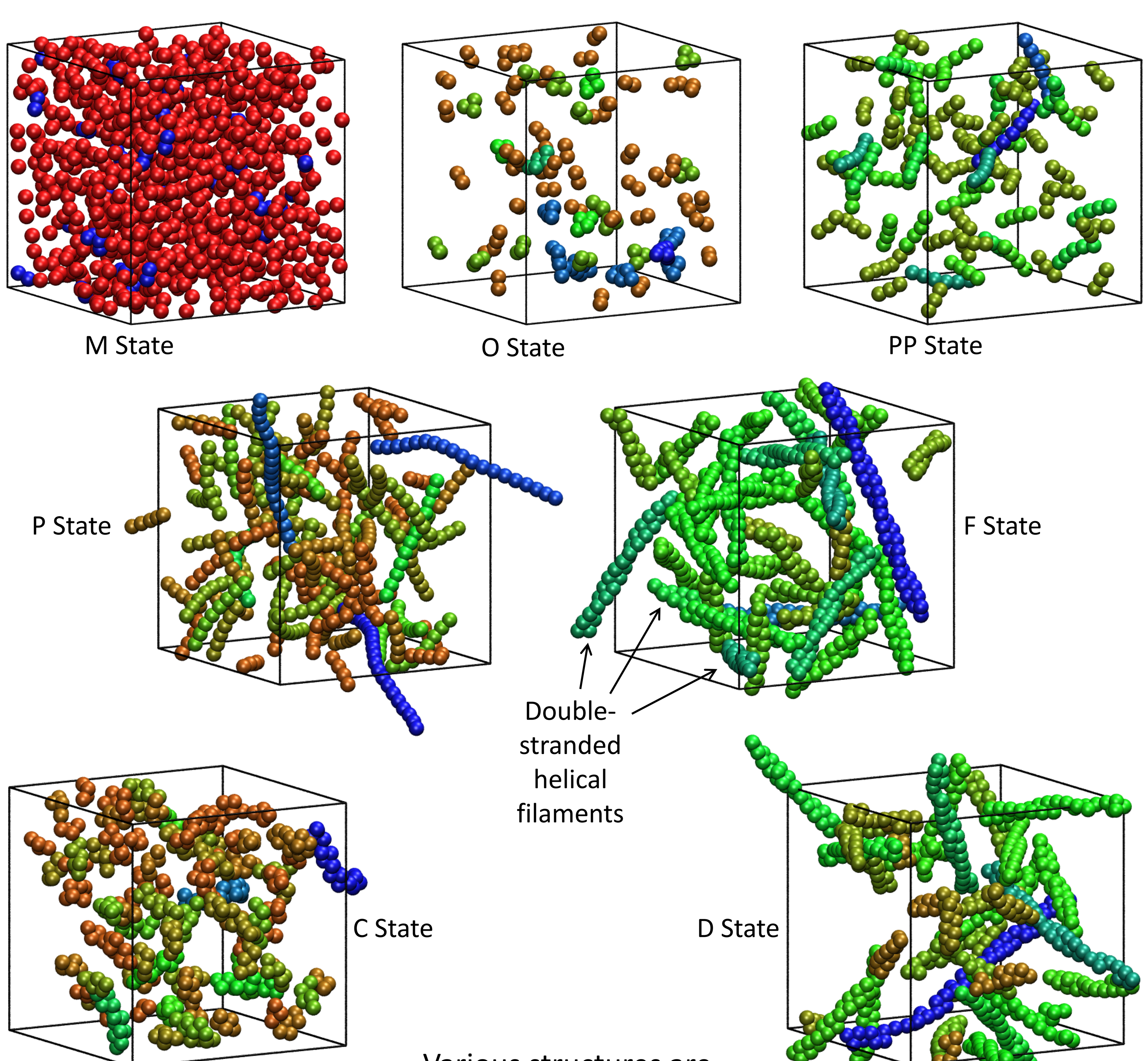
❑ Model to replicate F-actin geometry



- Rigid bent-rod monomers (core sites + attractive sites)
- Vertical bonding builds protofilaments while *staggered* lateral bonding links helices together
- Protofilaments have 12 monomers (n=12) per pitch; ideal filament/protofilament has *at least* 1 full pitch
- Bonding interactions only between attractive sites in the same color using soft cosine potential[2] – varying binding strength *A* leads to various structures

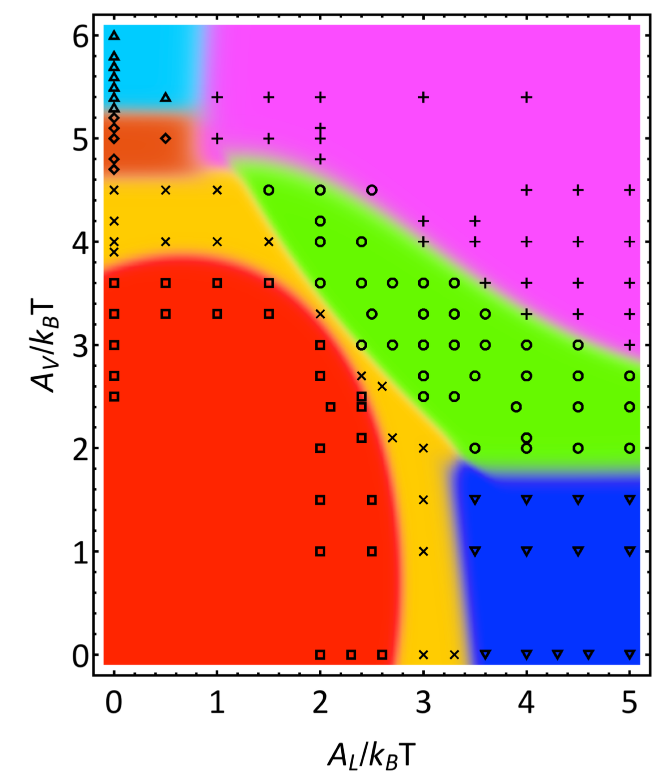
$$U(r) = -A\left[1+\cos\left(\frac{\pi r}{r_c}\right)\right] \qquad U(0) = -2A$$

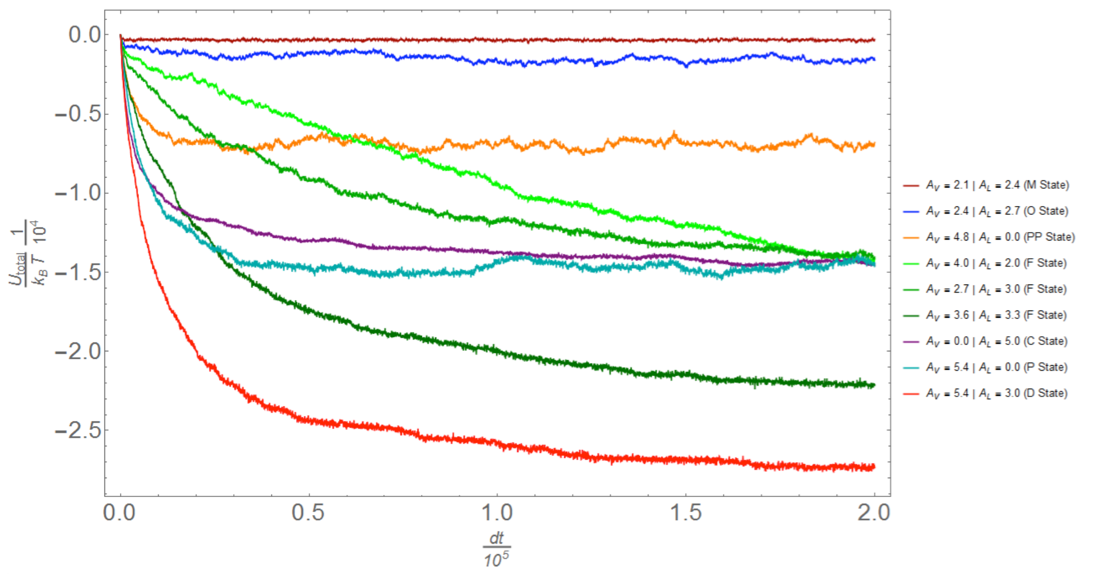
❑ Various self-assembled structures



Various structures are obtained by varying A_L and A_V

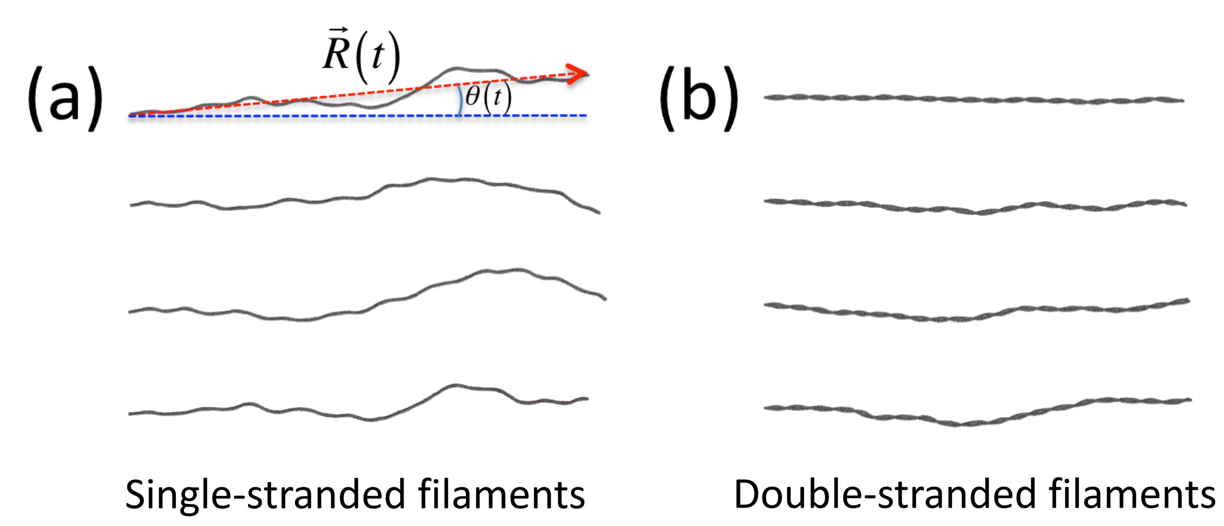
❑ Self-assembly structural diagram and assembly kinetics





Double-stranded actin-like filaments are formed when A_V and A_L are in the appropriate range (green zone in the structural diagram). Self-assembly mainly proceeds via an addition polymerization scheme: one monomer is added at a time. However, we also find oligomer addition and filament merging, though rarely.

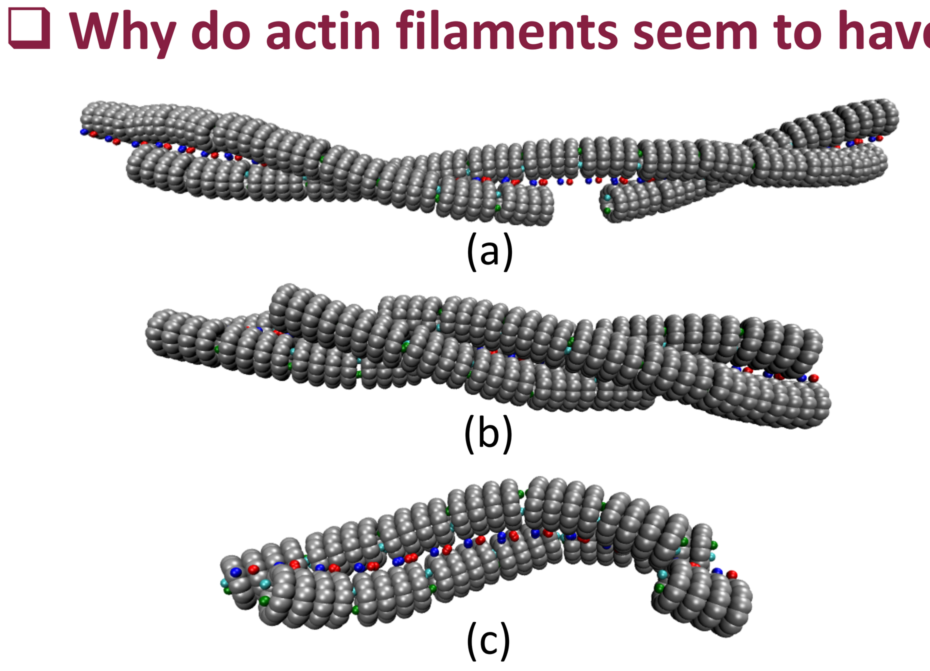
❑ Why are actin filaments double-stranded ?

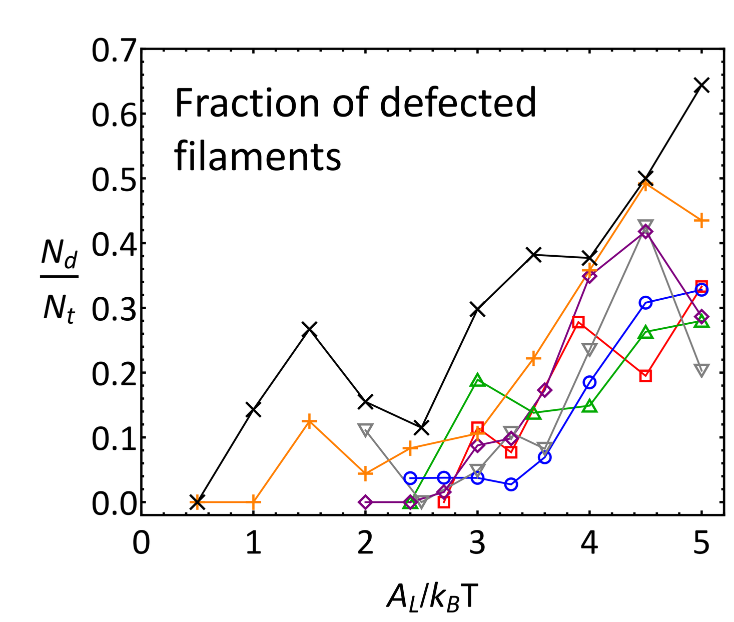


We model single- and double-stranded filaments built with bent-rod monomers. One end of each filament is fixed. The length and orientational fluctuations of the filaments are followed. Results (see the Table) show that the double-stranded filaments are more rigid structurally and exhibit much less fluctuations.

	A_L (k_BT)	A_V (k_BT)	<R> (σ)	ΔR (σ)	Δθ (°)
Single-stranded	0	7.5	391.76	29.19	1.82
	0	10.0	447.78	48.98	6.59
	0	15.0	455.37	25.62	5.47
Double-stranded	2.0	4.0	400.41	11.09	0.99
	2.7	3.6	435.36	14.89	1.33
	5.0	7.5	461.68	8.61	2.72

❑ Why do actin filaments seem to have $A_V > A_L$?





Three types of defects are observed for double-stranded actin-like filaments. The fraction of defected filaments starts to grow rapidly once $A_L > A_V$, which indicates that a high yield of actin filaments with a well-defined structure requires $A_V > A_L$.[1]

❑ References

1. O. N. Yogurtcu, J. S. Kim, and S. X. Sun, "*A mechanochemical model of actin filaments*", Biophysical Journal **104** (3), pp 737-738 (2013).
2. S. Cheng. A. Aggarwal, and M. J. Stevens, "*Self-assembly of artificial microtubules*", Soft Matter **8**, pp 5666-5678 (2012).

❑ Acknowledgments

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